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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,476	06/07/2000	Dennis A. Carson	103.021US1	1184

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EXAMINER	
KRASS, FREDERICK F	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/589,476	CARSON ET AL.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,11,13,14,26-29,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,11,13,14,26-29,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *A and B*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Case

All previous rejections are withdrawn.

New grounds of rejection follow. Since these were not necessitated by Applicant's amendment, this action is NON-FINAL.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 1, 3, 4, 13 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rephaeli (USP 5,939,455).

The prior art discloses the use of beta-oxidation inhibitors, e.g., etodolac and other NSAIDS (col. 4, line 24), as potentiating agents for butyric acid chemotherapeutic drugs. A wide range of cancers may be treated including multiple myeloma (col. 5, lines 34 and 35). The use of additional agents, e.g. butyric acids, is within the scope of the instant claims due to their use of the open-ended transitional phrase "comprising".

The prior art is not anticipatory insofar as the particular NSAID etodolac must be selected from a list of alternative potentiating agents, while multiple myeloma must be selected from a list of alternatively treatable cancers. It would have been obvious, however, to have chosen etodolac from one list and multiple myeloma from the other, given the unambiguous, specific, and discrete disclosure of each, consistent with the standard patent prosecution practice of interpreting prior art teachings for the entire scope of what is reasonably circumscribed within the four corners of the reference.

2) Claims 11, 14, 26-29 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rephaeli (USP 5,939,455) in view of WO 98/09603.

The primary reference is discussed in subsection "1)" supra, and differs from the instant claims insofar as it does not specify any particular enantiomer of etodolac. Administration is preferably oral (col. 16, lines 13 et seq.).

The secondary reference teaches that the R isomers of NSAIDS, including etodolac, are useful chemotherapeutic agents which have lower toxicities and side effects than their corresponding S isomers. See p. 7, lines 17-30 and p. 9, line 35. The secondary reference differs from the instant claims insofar as, although it suggests the treatment of "neoplastic disease" generally (p. 7, line 19), it does not specifically disclose multiple myeloma.

It would have been obvious to have used the R enantiomer of etodolac in the treatments of the primary reference, motivated by the desire to minimize toxicity and side effects as taught by the secondary reference. Furthermore, the selection of specific dosages (which in turn result in particular corresponding plasma levels) falling within those recited by instant claims 28 and 29 would have been obvious as well, motivated by the desire to provide the best treatment to those patients for whom those values would be optimal; the determination of optimal dosages in this manner is recognized by the primary reference at col. 15, lines 52-65 to be standard in the art, requiring the application of no more than routine experimentation. See also the passage spanning p. 11, line 26 to p. 12, line 12 of the secondary reference.

Obviousness-Type Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejections

1) Claims 1, 3, 4, 11, 13, 14, 26-29, 34 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting rejection as being unpatentable over claims 10, 13 and 15 of copending Application No. 09/634,207.

This is a provisional obviousness-type double patenting rejection.

2) Claims 1, 3, 4, 11, 13, 14, 26-29, 34 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting rejection as being unpatentable over claims 16-20 of copending Application No. 09/634,207 in view of Spiegelman et al (USP 6,552,055).

3) Claims 1, 3, 4, 11, 13, 14, 26-29, 34 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 and 12-23 of copending Application No. 10/682,790 in view of Spiegelman et al (USP 6,552,055).

This is a provisional obviousness-type double patenting rejection.

Discussion

Since the issues involved are largely cumulative, the three rejections above will be discussed together in the interest of economy.

USSN 10/682,790, USSN 09/634,207, and the instant application all plainly recite substantially overlapping methods of treatment using indole NSAID compounds, and R-etodolac in particular, to treat cancer, and multiple myeloma in particular.

The secondary reference, Spiegelman et al (USP 6,552,055), is cited to demonstrate the conventional nature of particular treatment features recited in various conflicting claims, e.g. determination of a suitable/optimal dosage range/concentration, administration via oral or parenteral routes, enteric coating to provide delayed release, etc. See the secondary reference at the passage spanning col. 17, line 22 to col. 18, line 40; and col. 21, lines 3-9. Note that multiple myeloma is recognized as a cancer "high" in PPAR-y, as it is described in the claims of the conflicting '790 application. (See, e.g., col. 9, lines 21-35 of the secondary reference). Similarly, the use of co-therapeutic agents to modify therapeutic response, including alkylating agents such as cyclophosphamide, is also well-known in the cancer art. (See col. 3, lines 39-45 and col. 16, lines 58-64).

The secondary reference is cited as demonstrating the state of the cancer art and as such is general in nature, differing from the instant claims insofar as it does not specify the use of etodolac

compounds. It does clearly support the well-established legal principle, however, that it is generally obvious to determine workable and/or optimal conditions for carrying out a claimed method using no more than routine experimentation. See for example In re Aller, 105 USPQ 233, 235 (1955). It would have been obvious to have determined workable and/or optimal dosages/concentrations, dosage routes and dosage forms, and to have modified such therapies with known co-therapeutic agents such as alkylating agents, motivated by the desire to provide the best treatment for a particular patient and/or condition. Such modifications are routine in the chemotherapeutic art as illustrated by Spiegelman et al and would require the application of no more than routine skill, consonant with the reasoning of the Aller decision.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 10:30AM- 7PM;
Tuesday: 10:30AM - 7PM;
Wednesday: off;
Thursday: 10:30AM- 7PM; and
Friday: 10:30AM-7PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614